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(54) Skin treatment method.

(57) A method of treating skin disorders such as acne vulgaris by applying topically to the epidermis a composition of an emulsion in which there is present a silane and a volatile low viscosity low molecular weight water immiscible liquid of a silicone fluid, causing the silane to penetrate follicular orifices, using the volatile silicone fluid for the purpose of driving the silane into sebaceous glands and destroying members of the staphylococcal group of bacteria therein. An abrasive, astringent and fragrance may also be included. This method also allows for the treatment of dermatosis, such as ring worm and athlete's foot.

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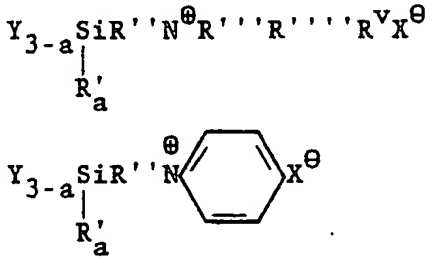
SKIN TREATMENT METHOD

Bound antimicrobials kill organisms on contact and continue to kill organisms without being diffused or leached from the surface. Thus, the bound antimicrobial leaves behind an effective level of active ingredient and is able to control a broad spectrum of microorganisms including gram negative and gram positive bacteria, mold, mildew, fungi, yeast and algae. An exemplary category of bound antimicrobial is an alkoxysilane quaternary ammonium compound and such alkoxysilane quaternary ammonium compounds have been found to be more effective at reducing the number of microorganisms and inhibiting microbially generated odors, than conventional organotin compounds and other organic quaternary ammonium compounds. The silanes of the present invention immobilize on surfaces and bond thereto to provide a coating of immobilized antimicrobial, unlike conventional materials.

In the present invention, this bound characteristic of alkoxysilane quaternary ammonium compounds, as well as their capabilities of performing at effective kill levels beyond prior art types of compositions, is taken advantage of in the treatment of skin disorders, in order to reduce or substantially eliminate the incidence of microorganisms, germs, their metabolic products and their somatic and reproductive cell parts, which contribute to the spread of such disorders.

This invention relates to a method of treating acne vulgaris of the skin by applying topically to the epidermis a composition of an emulsion including an antibacterially effective amount of a silane and a water immiscible liquid, causing the silane to penetrate follicular orifices, driving the silane into sebaceous glands and destroying members of the staphylococcal group of bacteria therein. The silane is an organosilicon quaternary ammonium compound and an organosilane having the general formula selected from the group consisting of



and

wherein, in each formula,

Y is R or RO where each R is an alkyl radical of 1 to 4 carbon atoms or hydrogen;

a has a value of 0, 1 or 2;

$\bar{R}'$ is a methyl or ethyl radical;

R'' is an alkylene group of 1 to 4 carbon atoms;

R''', R'''' and R^{v} are each independently selected from a group consisting of alkyl radicals of 1 to 18 carbon atoms, $-CH_2C_6H_5$, $-CH_2CH_2OH$, $-CH_2OH$ and $-(CH_2)_xNHC(O)R^{vi}$, wherein x has a value of from 2 to 10 and R^{vi} is a perfluoroalkyl radical having from 1 to 12 carbon atoms; and

X is chloride, bromide, fluoride, iodide, acetate or tosylate.

In a preferred embodiment, the water immiscible liquid is a polysiloxane selected from the group consisting of polysiloxanes having the general formula

$R'_3SiO(R''_2SiO)_w(R'''QSiO)_2SiR_p'3$ and $(R'R''SiO)_y$

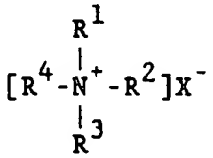
wherein R' is an alkyl radical of 1 to 3 carbon atoms, phenyl, an alkoxy radical having the formula $R''''O$-, wherein R'''' is an alkyl radical of 1 to 4 carbon atoms or hydrogen; R'' is an alkyl radical of 1 or 2 carbon atoms or the phenyl group; R''' has the same meaning as R''; Q is a substituted or unsubstituted radical composed of carbon and hydrogen or carbon, hydrogen and oxygen or carbon, hydrogen and sulfur or carbon, hydrogen and nitrogen; w has a value of from 1 to 500; z has a value of 1 to 25 and y has a value of 3 to 5.

The composition may also include an abrasive selected from the group consisting of pumice, talc, mica, iron oxide, titanium oxide, titanium dioxide, zinc oxide, kaolin, magnesium oxide, zinc stearate, magnesium stearate, starch, chalk, magnesium carbonate and boric acid. In addition, a fragrance may be added to the composition, as well as an astringent selected from the group consisting of alum, silver nitrate, aluminum

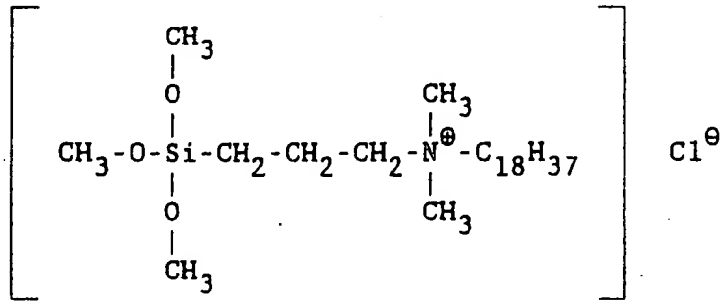
sulphate, aluminum chlorohydrate, zinc chloride, zinc chlorohydrate, aluminum-zirconium chlorohydrate, aluminum chlorohydroxide, zirconium hydroxychloride, aluminum hydroxychloride-zirconyl hydroxy oxychloride and aluminum-zirconium tetrachlorohydrexglycinate. In one particularly preferred embodiment, the polysiloxane is selected from the group consisting of polydimethylsiloxane, polyphenylmethylsiloxane and polydimethylcyclosiloxane. The compositions may take various forms ranging from emulsions and microemulsions to treated powders.

It is, therefore, an object of the present invention to provide a treatment method for skin disorders such as acne vulgaris in which an antimicrobial agent such as a bound type of silicone quaternary ammonium salt compound is caused to penetrate follicular openings of the skin areas sought to be treated whereby the antimicrobial agent actually enters within sebaceous glands in order to kill and immobilize microorganisms within the glands themselves of the Staphylococcus species of bacteria, for example. The driving force for causing the antimicrobial agent to penetrate downwardly within the sebaceous gland is provided by a highly volatile low viscosity low molecular weight silicone fluid such as siloxanes which are cyclics and polysiloxanes referred to hereinabove. These fluids carry the silicone quaternary ammonium antimicrobial compounds into contact with the bacteria which harbor within the regions of the gland and, hence, in addition to surface kill, provide an interior gland kill resulting in a more effective skin disorder treatment than known heretofore. Other penetrating assisting agents such as alcohols or dimethylformamide may also be used to assist in delivering the antimicrobial.

Ammonium compounds in which all of the hydrogen atoms on nitrogen have been substituted by alkyl groups are called quaternary ammonium salts. These compounds may be represented in a general sense by the formula:



The nitrogen atom includes four covalently bonded substituents that provide a cationic charge. The R groups can be any organic substituent that provides for a carbon and nitrogen bond with similar and dissimilar R groups. The counterion X is typically halogen. Use of quaternary ammonium compounds is based on the hydrophilic portion of the molecule which bears a positive charge. Since most surfaces are negatively charged, solutions of these cationic surface active agents are readily adsorbed to the negatively charged surface. This affinity for negatively charged surfaces is exhibited by 3-(trimethoxysilyl)-propyldimethyloctadecyl ammonium chloride of the formula:

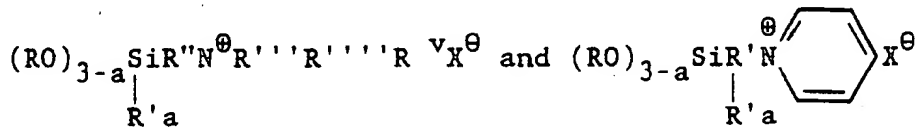


In the presence of moisture, this antimicrobial agent imparts a durable, wash resistant, broad spectrum biostatic surface antimicrobial finish to a substrate. The organosilicon quaternary ammonium compound is leach resistant, nonmigrating and is not consumed by microorganisms. It is effective against gram positive and gram negative bacteria, fungi algae, yeasts, mold, rot and mildew. The silicone quaternary ammonium salt provides durable, bacteriostatic, fungistatic and algistatic surfaces. It can be applied to organic or inorganic surfaces as a dilute aqueous or solvent solution of 0.1-1.5 percent by weight of active ingredient. After the alkoxysilane is applied to a surface, it is chemically bonded to the substrate by condensation of the silanol groups at the surface. The pure compound is crystalline whereas methanol solutions of the

compound are low viscosity, light to dark amber liquids, soluble in water, alcohols, ketones, esters, hydrocarbons and chlorinated hydrocarbons. The compound has been used in applications such as, for example, socks, filtration media, bed sheets, blankets, bedspreads, carpet, draperies, fire hose fabric materials, humidifier belts, mattress pads, health care apparel, mattress ticking, underwear, nonwoven disposable diapers, nonwoven fabrics, outerwear fabrics, nylon hosiery, vinyl paper, wallpaper, polyurethane cushions, roofing materials, sand bags, tents, tarpaulins, sails, rope, blood pressure cuffs, athletic and casual shoes, shoe insoles, shower curtains, toilet tanks, toilet seat covers, throw rugs, towels, umbrellas, upholstery fiberfill, intimate apparel, wiping cloths and medical devices such as blood pressure cuffs.

In the examples as well as in the tables, the composition identified as TMS refers to a product manufactured by the Dow Corning Corporation, Midland, Michigan, as an antimicrobial agent. This compound is 3-(trimethoxysilyl)-propyloctadecyldimethyl ammonium chloride referred to above diluted to forty-two percent active ingredients by weight with methanol.

The silanes useful in this invention have the general formula



It should be noted that generically, these materials are quaternary ammonium salts of silanes. Most of the silanes falling within the scope of this invention are known silanes and references disclosing such silanes are numerous. One such reference, United States Patent No. 4,259,103, issued to James R. Malek and John L. Speier, on March 31, 1981, discusses the use of such silanes to render the surfaces of certain substrates antimicrobial. British Patent No. 1,433,303, issued to Charles A. Roth shows the use of fillers treated with certain silanes to be used in paints and the like to give antimicrobial effects.

Numerous other publications have disclosed such silanes, namely, A. J. Isquith, E. A. Abbott and P. A. Walters, Applied Microbiology, December, 1972, pages 859-863; P. A. Walters, E. A. Abbott and A. J. Isquith, Applied Microbiology, 25, No. 2, p. 253-256, February 1973 and E. A. Abbott and A. J. Isquith, United States Patent No. 3,794,736 issued February 26, 1974, U.S. Patent No. 4,406,892, issued September 27, 1983, among others.

For purposes of this invention, the silanes can be used neat or they can be used in solvent or aqueous-solvent solutions. When the silanes are used neat, the inventive process is preferably carried out in a system in which some small amount of water is present. If it is not possible to have a system with some small amount of water present, then a water soluble or water-dispersable, low molecular weight hydrolyzate of the silane may be used. What is important is the fact that the durability of any effect produced by the silane as part of a product requires that the silane molecule react with a surface to a certain extent. The most reactive species, as far as the silanes are concerned, is the $\equiv$SiOH that is formed by hydrolysis of the alkoxy groups present on the silane. The $\equiv$SiOH groups tend to react with the surface and bind the silanes to the surface. It is believed by the inventor that even though the prime mode of coupling to the surface system is by the route described above, it is also believed by the inventor that the alkoxy groups on the silicon atom may also participate in their own right to bind to the surface.

Preferred for this invention is a reactive surface containing some small amount of water. By "reactive", it is meant that the surface must contain some groups which will react with some of the silanols generated by hydrolysis of the silanes of this invention.

R in the silanes of this invention are alkyl groups of 1 to 4 carbon atoms. Thus, useful as R in this invention are the methyl, ethyl, propyl and butyl radicals. In the above formulas, RO can also be R. R can also be hydrogen thus indicating the silanol form, i.e. the hydrolyzate. The value of a is 0, 1 or 2 and R' is a methyl or ethyl radical.

R'' for purposes of this invention is an alkylene group of 1 to 4 carbon atoms. Thus, R'' can be alkylene groups such as methylene, ethylene, propylene and butylene. R''', R'''' and R^{v} are each independently selected from a group which consists of alkyl radicals of 1 to 18 carbons, $-CH_2C_6H_5$, $-CH_2CH_2OH$, $-CH_2OH$ and $-(CH_2)_xNHC(O)R^{vi}$. x has a value of from 2 to 10 and R^{vi} is a perfluoroalkyl radical having from 1 to 12 carbon atoms. X is chloride, bromide, fluoride, iodide, acetate or tosylate.

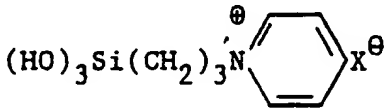
Preferred for this invention are the silanes of the general formula

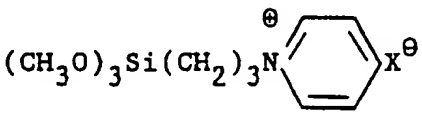
wherein
R is methyl or ethyl; a has a value of zero; R'' is propylene; R''' is methyl or ethyl; R'''' and R^{v} are selected from alkyl groups containing 1 to 18 carbon atoms wherein at least one such group is larger than eight carbon atoms and x is either chloride, acetate or tosylate.

Most preferred for this invention are those silanes having the formula
$(CH_3O)_3Si(CH_2)_3N^{\oplus}(CH_3)_2C_{18}H_{37}Cl^-$ and $(CH_3O)_3Si(CH_2)_3$ -$N^{\oplus}CH_3(C_{10}H_{21})_2Cl^-$.

As indicated above, most of these silanes are known from the literature and methods for their preparation are known as well. See, for example, U.S. Patent 4,282,366, issued August 4, 1981; U.S. Patent 4,394,378, issued July 19, 1983, and U.S. Patent 3,661,963 issued May 9, 1972, among others.

Specific silanes within the scope of the invention are represented by the formulae:
$(CH_3O)_3Si(CH_2)_3N^{*}(CH_3)_2C_{18}H_{37}Cl^-$,
$(CH_3O)_3Si(CH_2)_3N^{*}(CH_3)_2C_{18}H_{37}Br^-$,
$(CH_3O)_3Si(CH_2)_3N^{*}(C_{10}H_{21})_2CH_3Cl^-$,
$(CH_3O)_3Si(CH_2)_3N^{*}(C_{10}H_{21})_2CH_3Br^-$,
$(CH_3O)_3Si(CH_2)_3N^{*}(CH_3)_3Cl^-$,
$(CH_3O)_3SiCH_2CH_2CH_2P^{*}(C_6H_5)_3Cl^-$,
$(CH_3O)_3SiCH_2CH_2CH_2P^{*}(C_6H_5)_3Br^-$,
$(CH_3O)_3SiCH_2CH_2CH_2P^{*}(CH_3)_3Cl^-$,
$(CH_3O)_3SiCH_2CH_2CH_2P^{*}(C_6H_{13})_3Cl^-$,
$(CH_3)_3Si(CH_2)_3N^{*}(CH_3)_2C_{12}H_{25}Cl^-$,
$(CH_3)_3Si(CH_2)_3N^{*}(C_{10}H_{21})_2CH_3Cl^-$,
$(CH_3)_3Si(CH_2)_3N^{*}(CH_3)_2C_{18}H_{37}Cl^-$,
$(CH_3O)_3Si(CH_2)_3N^{*}(CH_3)_2C_4H_9Cl^-$,
$(C_2H_5O)_3Si(CH_2)_3N^{*}(CH_3)_2C_{18}H_{37}Cl^-$,
$(CH_3O)_3Si(CH_2)_3N^{*}(CH_3)_2CH_2C_6H_5Cl^-$,
$(CH_3O)_3Si(CH_2)_3N^{*}(CH_3)_2CH_2CH_2OHCl^-$,





$(CH_3O)_3Si(CH_2)_3N^{*}(CH_3)_2(CH_2)_3NHC(O)(CF_2)_6CF_3Cl^-$, $(CH_3O)_3Si(CH_2)_3N^{*}(C_2H_5)_3Cl^-$.

The water immiscible liquids or volatiles, as used in the present invention, are silicone oils which are highly volatile and low in viscosity and molecular weight. For example, there may be employed trimethylsiloxy endblocked polydimethylsiloxanes, cyclic siloxanes such as dimethylsiloxane cyclic tetramer and phenylmethyl fluids such as linear polyphenylmethylsiloxanes. Preferred for this invention are those silicone oils having a viscosity at 25° C. ranging from about 0.65 cs to about one thousand cs. A particularly preferred range is from about 0.65 cs to about 20 cs, although those silicone oils of viscosities of 50 cs and 350 cs can be employed. These silicone oils are more particularly described and set forth in detail in U.S. Patent No. 4,631,273, issued December 23, 1986. Such silicone oils are siloxanes which are low molecular weight cyclics and polysiloxanes having the general formula
$R'_3SiO(R''_2SiO)_w(R''QSiO)_2SiR_p'3$ and $(R'R''SiO)_y$
wherein R' is an alkyl radical of 1 to 3 carbon atoms, phenyl, an alkoxy radical having the formula R''''O-, wherein R'''' is an alkyl radical of 1 to 4 carbon atoms or hydrogen; R'' is an alkyl radical of 1 or 2 carbon

atoms or the phenyl group; R‴ has the same meaning as R″; Q is a substituted or unsubstituted radical composed of carbon and hydrogen or carbon, hydrogen and oxygen or carbon, hydrogen and sulfur or carbon, hydrogen and nitrogen; w has a value of from 1 to 500; z has a value of 1 to 25 and y has a value of 3 to 5.

As is well known, skin covers the human body and furnishes a protective covering for deeper tissues. It also serves as a barrier to prevent entry of infectious organisms which inhabit the skin surface. Skin performs important excretory functions by means of the sweat and sebaceous glands and contains not only sweat and sebaceous glands but also hair follicles and sensory nerve endings of various kinds. The skin is made up of two layers including the deep or corium layer and the superficial or epidermis layer. The hairs are divided into the root and the shaft with the root being embedded in the hair follicle while the shaft is the free portion. Sebaceous glands exist wherever there are hairs. Ducts of the sebaceous glands open into the superficial parts of the hair follicles and vary in number for each follicle from one to four. The deep ends of the glands expand and contain droplets of oil which are liberated into the hair follicle. It is therefore possible for surface microorganisms to work their way downwardly through the follicular openings and into the sebaceous glands, gradually penetrating the expanded portion of the gland. It is these penetrating microorganisms, as well as those surface varieties, toward which the present invention is particularly directed.

Acne is any inflammatory disease of the sebaceous glands. Acne vulgaris is common acne and is a chronic inflammatory disease of the sebaceous glands seen most often on the face, back and chest. The inflamed glands form small pink papules some of which surround comedones or blackheads or take the form of small pustules. Bacterial infections of the skin and its subjacent soft tissues may be generalized or localized, acute, subacute or chronic. Such infections are most often pyogenic and pus forming. The most frequent pyogenic infections including acne and acne vulgaris are caused by members of the Staphylococcal group of bacteria. Although many treatments of such diseases are known as noted hereinabove, none is known heretofore which will rid the sebaceous gland interiors of these Staphylococcal bacterial invaders. Thus, in accordance with the present invention, the water immiscible liquid, being highly volatile, carries the silane antimicrobial compound of the present invention downwardly into the interiors of the sebaceous glands wherein the bound antimicrobial compound kills or inhibits the proliferation of bacteria of the Staphylococcal group, as well as killing surface microorganisms. In combination with the water immiscible fluid, the antimicrobial agents of the present invention possess a penetrating power and permanence not heretofore known.

In the method of treating acne vulgaris in accordance with the present invention there is applied topically to the epidermis a composition of an emulsion including an antibacterially effective amount of a silane and a water immiscible liquid. The emulsion, its ingredients and preparation, are disclosed in detail in U.S. Patent No. 4,631,273. The composition may also include in addition to the silane and water immiscible liquid, an abrasive selected from the group consisting of pumice, talc, mica, iron oxide, titanium oxide, titanium dioxide, zinc oxide, kaolin, magnesium oxide, zinc stearate, magnesium stearate, starch, chalk, magnesium carbonate and boric acid. In addition, there may be included an astringent selected from the group consisting of alum, silver nitrate, aluminum sulphate, aluminum chlorohydrate, zinc chloride, zinc chlorohydrate, aluminum-zirconium chlorohydrate, aluminum chlorohydroxide, zirconium hydroxychloride, aluminum hydroxychloride-zirconyl hydroxy oxychloride and aluminum-zirconium tetrachlorohydrex-glycinate.

The compositions of the present invention may include any type of fragrance, cologne or perfume, compatible with the materials. For example, the fragrance may be a natural product such as Ambergris, Benzoin, Civet, Clove Leaf Oil, Galbanum, Jasmine Absolute, Labdanum, Mate', Melilot, Mimosa, Musk Tonquin, Myrrh, Mousse de Chene, Olibanum, Opopanax, Orris, Patchouli, Rosemary Oil, Sandalwood Oil, Vetivert Oil and Violet Leaves Absolute. Among the various aroma chemicals that may be employed in addition to the foregoing natural products are, for example, acetylated cedarwood terpenes, amylcinnamic aldehyde, amyl salicylate, methyl salicylate, benzyl acetate, benzyl salicylate, p-tert-butylcyclohexyl acetate, citronellol, coumarin, Galaxolide, geraniol, hexylcinnamic aldehyde, isobornyl acetate, linalool, linalyl acetate, Lyral, musk ambrette, phenethyl alcohol, tetrahydromuguol and terpinyl acetate. Fragrances that have become classics as descriptors for other fragrances in the same family are also included herein and would comprehend the Straight Floral Family, Floral Bouquet Family, Aldehydic Floral Family, Oriental Family, Chypre Family, Woody Family, Green Family, Citrus Family, Fougere Family, Canoe Family, Husk Family, Animal Family, Leather Family, Spice Family and the Herbal Family.

Preferred fragrances include Citronellol, Cineole, YSL PARIS®, manufactured by Charles of the Ritz Group of New York, New York; JOY®, manufactured by Jean Patou, Inc. of New York, New York; OSCAR de la RENTA®, manufactured by Oscar de la Renta, Ltd. of New York, New York; and IVOIRE de

BALMAIN™, manufactured by Balmain International B. V. of Rotterdam, Netherlands.

The following example relates to a test conducted on carpet samples treated with TMS in order to show the efficacy of this antimicrobial agent against the bacterial microorganism Staphylococcus aureus.

Example I

In order to demonstrate the effectiveness of TMS against the bacteria Staphylococcus aureus, nylon surfaces were treated with the antimicrobial agent and the results are tabulated in Tables I to VIII. Comparisons were made on untreated as well as treated surfaces, in order to show the effect of TMS in inhibiting and inactivating test microbes applied to the surfaces. Four types of nylon material surfaces were selected for the tests, including a high-pile cut, a fine velour, a light loop fabric and a heavy-duty loop fabric. Durability of treatment was shown by testing each surface type in its new condition and after 7, 14 and 21 shampoo treatments. For the shampoo treatments, a commercial spray extraction device was used and a non-bacterial shampoo having active groups of nonionic surfactants and phosphates. Each test was repeated three times in order to verify the results obtained.

Test surfaces 50 mm x 50 mm were used as microbe carrier. To prewet the surface, the surface was immersed at 37° C. into a phosphate buffer solution, removed, placed between sterile filter papers in order to remove excess fluid and placed in sterile Petri dishes. Test microbes suspensions were obtained from a nutrient bouillon incubated for 18 hours at 37° C. and stirred at a frequency of 120 rpm by transferring 1 ml of culture bouillon into 9 ml of phosphate buffer. From this 1:10 dilution, a 1:100 dilution was made by placing 1 ml from the first dilution into 9 ml of phosphate buffer. Using the same procedure, a 1:1000 dilution of the suspension was formed. The 1:1000 dilution was used to inoculate the test pieces in sterile Petri dishes by applying 0.01 ml along each lateral edge and diagonally or a total of 0.05 ml of test microbial suspension per microbial carrier. The inoculated pieces were placed into sealed Petri dishes in an air-tight container which was filled to 10% of its volume with water and preheated to 37° C. Incubation of the test pieces was conducted at 37° C. in the container for 4 hours.

The microbial carrier was removed from the container and placed into covered glasses with 200 ml capacity and filled with 100 ml of Letheen broth and shaken for 10 minutes on a shaking device with a frequency of 180 rpm. Reisolation of the test microbes was carried out by transferring 1 ml from the Letheen broth directly into a Petri dish followed by one dilution with Letheen broth 1:10 and 1:100. 1 ml of each of the dilutions was placed into a Petri dish and covered with microbial nutrient agar. The incubation time was 24 hours at 37° C. The grown colony forming units were then counted.

Results are shown in Tables I - VIII in logarithmic figures and each Table refers to one piece of carpeting. The dilution stages are included so that a possible total microbial reduction is not expressed as such, but rather defined as "reduction>". In ascertaining reduction, the largest reduction value was selected from the absolute figures of the dilution stages of reisolation, converted into logarithms and subtracted from the microbial seed. Treated carpet is durable since even the high number of shampooing treatments had no significant effect on the microbial reduction rates.

With high pile cut carpet an above-average inoculation with microbes such as Staphylococcus aureus led to reisolation of test microbes on microbial carriers treated with TMS. For fine velour, with Staphylococcus aureus on treated microbial carriers, the test microbe species were reisolated. The reduction rates in the microbial carriers of which Staphylococcus aureus was reisolated were above 4 log stages. The treated light loop fabric behaved as the fine velour. Staphylococcus aureus was reisolated on treated microbial carriers and a microbial reduction of more than 4 log stages was established. Staphylococcus aureus was reisolated from the treated heavy-duty loop fabric. The microbial reduction rates for Staphylococcus aureus was between 3.85 and 3.91 log stages.

TABLE I

STAPHYLOCOCCUS AUREUS							
MICROBIAL GROWTH REDUCTION OF TREATED AND UNTREATED HIGH-PILE CUT NYLON TEST SURFACES							
Shampoo Treatments	Legend	Untreated			TMS Treated		
		Run 1	Run 2	Run 3	Run 1	Run 2	Run 3
0	A	6.47	6.32	6.25	6.47	6.32	6.25
	B	4.30	4.06	3.98	2.60	2.30	2.00
	C	2.17	2.26	3.27	3.87	4.02	4.25
7	A	5.91	5.86	5.76	5.91	5.86	5.76
	B	4.04	4.03	3.99	2.30	2.30	2.00
	C	1.87	1.83	1.77	3.61	3.56	3.76
14	A	5.66	5.59	5.62	5.66	5.59	5.62
	B	3.86	3.76	3.37	2.47	U	U
	C	1.80	1.83	1.83	3.19	>3.59	>3.62
21	A	5.81	5.77	5.69	5.81	5.77	5.69
	B	3.99	3.93	3.91	U	U	U
	C	1.82	1.84	1.78	>3.81	>3.77	>3.69

A = Microbial inocculation

B = Reisolation

C = Reduction

U = No microbes reisolatable. Value below limit of detection of two-log stages.

TABLE II

STAPHYLOCOCCUS AUREUS							
MICROBIAL GROWTH REDUCTION OF TREATED AND UNTREATED HIGH-PILE CUT NYLON TEST SURFACES							
Shampoo Treatments	A	Untreated			TMS Treated		
		Run 1	Run 2	Run 3	Run 1	Run 2	Run 3
0	B	6.47	6.32	6.25	6.47	6.32	6.25
	10-2	204	116	96	4	2	1
	10-3	23	16	9	0	0	0
	10-4	2	1	1	0	0	0
7	B	5.91	5.86	5.76	5.91	5.86	5.76
	10-2	110	108	99	2	2	1
	10-3	12	11	9	0	0	0
	10-4	2	3	0	0	0	0
14	B	5.66	5.59	5.62	5.66	5.59	5.62
	10-2	73	58	54	3	0	0
	10-3	9	7	4	0	0	0
	10-4	0	0	0	0	0	0
21	B	5.81	5.77	5.69	5.81	5.77	5.69
	10-2	99	87	82	0	0	0
	10-3	11	9	10	0	0	0
	10-4	2	1	2	0	0	0

A = Microbial inocculation (log). Reisolation per microbial carrier in dilution stage.

B = Microbial inocculation

TABLE III

STAPHYLOCOCCUS AUREUS							
MICROBIAL GROWTH REDUCTION OF TREATED AND UNTREATED NYLON FINE VELOUR TEST SURFACES							
Shampoo Treatments	Legend	Untreated			TMS Treated		
		Run 1	Run 2	Run 3	Run 1	Run 2	Run 3
0	A	6.47	6.32	6.25	6.47	6.32	6.25
	B	4.27	4.21	4.19	2.30	2.00	2.00
	C	2.20	2.12	2.06	4.17	4.32	4.25
7	A	5.91	5.86	5.76	5.91	5.86	5.76
	B	3.99	3.72	3.71	U	U	U
	C	1.92	2.14	2.05	>3.91	>3.86	>3.76
14	A	5.66	5.59	5.62	5.66	5.59	5.62
	B	3.66	3.55	3.64	U	U	U
	C	2.00	2.04	1.98	>3.66	>3.59	>3.62
21	A	5.81	5.77	5.69	5.81	5.77	5.69
	B	3.97	3.91	3.80	U	U	U
	C	1.84	1.86	1.89	>3.81	>3.77	>3.69

A = Microbial inocculation

B = Reisolation

C = Reduction

U = No microbes reisolatable. Value below limit of detection of two-log stages.

TABLE IV

STAPHYLOCOCCUS AUREUS							
MICROBIAL GROWTH REDUCTION OF TREATED AND UNTREATED NYLON FINE VELOUR TEST SURFACES							
Shampoo Treatments	A	Untreated			TMS Treated		
		Run 1	Run 2	Run 3	Run 1	Run 2	Run 3
0	B	6.47	6.32	6.25	6.47	6.32	6.25
	10-2	188	163	156	2	1	1
	10-3	16	14	14	0	0	0
	10-4	1	1	1	0	0	0
7	B	5.91	5.86	5.76	5.91	5.86	5.76
	10-2	98	53	52	0	0	0
	10-3	11	6	7	0	0	0
	10-4	0	0	0	0	0	0
14	B	5.66	5.59	5.62	5.66	5.59	5.62
	10-2	46	36	44	0	0	0
	10-3	3	3	2	0	0	0
	10-4	0	0	0	0	0	0
21	B	5.81	5.77	5.69	5.81	5.77	5.69
	10-2	94	83	64	0	0	0
	10-3	11	7	7	0	0	0
	10-4	2	0	0	0	0	0

A = Microbial inocculation (log). Reisolation per microbial carrier in dilution stage.

B = Microbial inocculation

TABLE V

STAPHYLOCOCCUS AUREUS							
MICROBIAL GROWTH REDUCTION OF TREATED AND UNTREATED NYLON LIGHT LOOP FABRIC TEST SURFACES							
Shampoo Treatments	Legend	Untreated			TMS Treated		
		Run 1	Run 2	Run 3	Run 1	Run 2	Run 3
0	A	6.47	6.32	6.25	6.47	6.32	6.25
	B	4.09	4.03	3.96	2.30	2.30	2.00
	C	2.38	2.29	2.29	4.17	4.17	4.25
7	A	5.91	5.86	5.76	5.91	5.86	5.76
	B	3.94	3.82	3.77	U	U	U
	C	1.97	2.04	1.99	>3.91	>3.86	>3.76
14	A	5.66	5.59	5.62	5.66	5.59	5.62
	B	3.66	3.56	3.61	U	U	U
	C	2.00	2.03	2.01	>3.66	>3.59	>3.62
21	A	5.81	5.77	5.69	5.81	5.77	5.69
	B	3.69	3.66	3.59	U	U	U
	C	2.12	2.11	2.10	>3.81	>3.77	>3.69

A = Microbial inocculation

B = Reisolation

C = Reduction

U = No microbes reisolatable. Value below limit of detection of two-log stages.

TABLE VI

STAPHYLOCOCCUS AUREUS							
MICROBIAL GROWTH REDUCTION OF TREATED AND UNTREATED NYLON LIGHT LOOP FABRIC TEST SURFACES							
Shampoo Treatments	A	Untreated			TMS Treated		
		Run 1	Run 2	Run 3	Run 1	Run 2	Run 3
0	B	6.47	6.32	6.25	6.47	6.32	6.25
	10-2	125	108	93	2	2	1
	10-3	19	14	12	0	0	0
	10-4	3	0	2	0	0	0
7	B	5.91	5.86	5.76	5.91	5.86	5.76
	10-2	88	67	59	0	0	0
	10-3	12	8	4	0	0	0
	10-4	2	0	0	0	0	0
14	B	5.66	5.59	5.62	5.66	5.59	5.62
	10-2	46	37	41	0	0	0
	10-3	5	2	4	0	0	0
	10-4	0	0	0	0	0	0
21	B	5.81	5.77	5.69	5.81	5.77	5.69
	10-2	49	46	39	0	0	0
	10-3	6	7	4	0	0	0
	10-4	0	0	0	0	0	0

A = Microbial inocculation (log). Reisolation per microbial carrier in dilution stage.

B = Microbial inocculation

TABLE VII

STAPHYLOCOCCUS AUREUS							
MICROBIAL GROWTH REDUCTION OF TREATED AND UNTREATED NYLON HEAVY-DUTY LOOP FABRIC TEST SURFACES							
Shampoo Treatments	Legend	Untreated			TMS Treated		
		Run 1	Run 2	Run 3	Run 1	Run 2	Run 3
0	A	6.47	6.32	6.25	6.47	6.32	6.25
	B	3.97	3.91	3.74	2.60	2.47	U
	C	2.50	2.41	2.51	3.87	3.85	>4.25
7	A	5.91	5.86	5.76	5.91	5.86	5.76
	B	3.98	3.96	3.64	2.00	2.00	U
	C	1.93	1.90	1.92	3.91	3.86	>3.76
14	A	5.66	5.59	5.62	5.66	5.59	5.62
	B	3.83	3.74	3.79	U	U	U
	C	1.83	1.85	1.83	>3.66	>3.59	>3.62
21	A	5.81	5.77	5.69	5.81	5.77	5.69
	B	3.83	3.79	3.59	U	U	U
	C	1.98	1.98	2.10	>3.81	>3.77	>3.81

A = Microbial inocculation
B = Reisolation
C = Reduction
U = No microbes reisolatable. Value below limit of detection of two-log stages.

TABLE VIII

STAPHYLOCOCCUS AUREUS							
MICROBIAL GROWTH REDUCTION OF TREATED AND UNTREATED NYLON HEAVY-DUTY LOOP FABRIC TEST SURFACES							
Shampoo Treatments	A	Untreated			TMS Treated		
		Run 1	Run 2	Run 3	Run 1	Run 2	Run 3
0	B	6.47	6.32	6.25	6.47	6.32	6.25
	10-2	94	83	56	4	3	0
	10-3	11	9	7	0	0	0
	10-4	2	2	0	0	0	0
7	B	5.91	5.86	5.76	5.91	5.86	5.76
	10-2	96	93	44	1	1	0
	10-3	13	11	5	0	0	0
	10-4	2	1	0	0	0	0
14	B	5.66	5.59	5.62	5.66	5.59	5.62
	10-2	68	56	62	0	0	0
	10-3	7	7	8	0	0	0
	10-4	0	0	0	0	0	0
21	B	5.81	5.77	5.69	5.81	5.77	5.69
	10-2	69	62	39	0	0	0
	10-3	9	7	5	0	0	0
	10-4	1	0	0	0	0	0
A = Microbial inocculation (log). Reisolation per microbial carrier in dilution stage.							
B = Microbial inocculation							

The anion of an aqueous sodium salt of bromphenol blue can be complexed with the cation of polymerized silanes of this invention while on a substrate. The blue colored complex, substantive to a water rinse, is qualitatively indicative of the presence of the cation on the substrate thus indicating the extent of antimicrobial agent on a given substrate. A comparison of the intensity of retained blue color to a color standard is used as a check to determine if the treatment has been applied properly.

One method consists of preparing a 0.02 to 0.04 weight percent solution of bromphenol blue in distilled water. This solution is made alkaline using a few drops of saturated Na_2CO_3 solution per 100 milliliters of the solution. Two to three drops of this solution are placed on the treated substrate and allowed to stand for two minutes. The substrate is then rinsed with copious amounts of tap water and the substrate is observed for a blue stain and it is compared to a color standard.

For a spectrophotometric determination, the following test is used. The sodium salt of bromphenol blue is depleted from a standard solution by complexing with the cations on a treated substrate. The change in bromphenol blue concentration is determined spectrophotometrically or by comparison with color standards whereby the level of substrate treatment by the cationic silane is determinable.

The method consists of preparing a 0.02 weight percent standard solution of bromphenol blue in distilled water. It is made alkaline with a few drops of saturated Na_2CO_3 solution per 100 milliliters of bromphenol blue solution. The color of this solution is purple. The blank solution is adjusted to yield a 10 to 12% transmittance reading when measured in 1 cm cells using a spectrophotometer set at 589 nm by the following method. Fill a container 3/4 full of distilled water and add 2 ml of the 0.02% standard bromphenol blue solution for every 50 ml of distilled water. Add 0.5 ml of a 1% Triton® X-100 surfactant (manufactured by Rohm and Haas, Philadelphia, PA, USA) aqueous solution for every 50 ml of water. Mix and, using the spectrophotometer, determine the maximum absorbance. Adjust the upper zero to 100% transmittance with distilled water. Check the percent transmittance of the working bromphenol blue solution at the maximum absorbance setting. Adjust the blank solution to 10 to 12% transmittance with either water or bromphenol blue standard solution as necessary.

The samples of treated substrate can be tested by placing 0.5 gram samples of the substrate standards in a flask large enough for substantial agitation of the sample and the test solution. Add 50 ml of the working solution. Agitate for 20 minutes on a wrist-action shaker. Fill the test curvette with the test solution. Centrifuge if particulate matter is present. Measure the transmittance at the wavelength set forth above. The transmittance is compared against a standard curve prepared by preparing several substrate samples of known concentration of the cationic silane. For example, samples containing a known amount of cationic silane at, for example, 0%, 0.25%, 0.50%, 0.75% and 1% are read spectrophotometrically and a curve is plotted.

The antimicrobial activity of a treated surface is normally evaluated by shaking a sample weighing 0.75 grams in a 750,000 to 1,500,000 count Klebsiella pneumoniae suspension for a one hour contact time. The suspension is serially diluted, both before and after contact and cultured. The number of viable organisms in the suspensions is determined. The percent reduction based on the original count is determined. The method is intended for those surfaces having a reduction capability of 75 to 100% for the specified contact time. The results are reported as the percent reduction. Media used in this test are nutrient broth, catalog No. 0003-01-6 and tryptone glucose extract agar, catalog No. 0002-01-7 both available from Difco Laboratories, Detroit, Michigan, U.S.A. The microorganism used is Klebsiella pneumoniae American Type Culture Collection; Rockville, Md. U.S.A., catalog No. 4352. The procedure used for determining the zero contact time counts is carried out by utilizing two sterile 250 ml. screw-cap Erlenmeyer flasks for each sample. To each flask is added 70 ml of sterile buffer solution. To each flask is added, aseptically, 5 ml of the organism inoculum. The flasks are capped and placed on a wrist action shaker. They are shaken at maximum speed for 1 minute. Each flask is considered to be at zero contact time and is immediately subsampled by transferring 1 ml of each solution to a separate test tube containing 9 ml of sterile buffer. The tubes are agitated with a vortex mixer and then 1 ml of each solution is transferred to a second test tube containing 9 ml of sterile buffer. Then, after agitation of the tubes, 1 ml of each tube is transferred to a separate sterile petri dish. Duplicates are also prepared. Sixteen ml of molten (42° C.) tryptone glucose extract agar is added to each dish. The dishes are each rotated ten times clockwise and ten times counterclockwise. The dishes are then incubated at 37° C. for 24 to 36 hours. The colonies are counted considering only those between 30 and 300 count as significant. Duplicate samples are averaged. The procedure used for determining the bacterial count after 1 hour is essentially the same as that used to determine the count at the zero contact time. The only difference is that pour plating is performed at the 10^0 and 10^{-1} dilutions as well as at the 10^{-2} dilution. "Percent reduction" is calculated by the formula

$$\%R = \frac{\frac{B+C}{2} - A}{\frac{B+C}{2}} 100$$

where A is the count per milliliter for the flask containing the treated substrate; B is zero contact time count per milliliter for the flask used to determine "A" before the addition of the treated substrate and C is zero contact time count per milliliter for the untreated control substrate.

Example II

Antimicrobial activity against common skin isolates was determined using TMS coated (0.42% by weight) orlon nylon fabric. Evaluations were done using American Association of Textile Chemists and Colorists - 100-1977 test. Four swatches of test fabric were placed in the bottom of a milk dilution bottle; one ml of a 1×10^5 - 5×10^5/ml titer of the test organisms were padded onto the test fabrics; the test bottle was incubated for six hours at 37° C.; a neutralizing (Letheen broth) recovery solution was added, shaken; standard pour plate counts made using tryptic soy agar; incubated at 37° C. for 18-20 hours; and standard counts were made. Percent reductions were calculated as compared to the organisms retrieved from untreated orlon nylon fabric. Significant reduction of all test bacteria is demonstrated with up to five logs of reduction demonstrated, as seen in Table IX.

TABLE IX

TMS ACTIVITY AGAINST SKIN ISOLATES		
Skin Isolated Test Organism	Gram Stain	% Bacterial Reduction
Micrococcus sp. (I)	+	99.0
Staphylococcus epidermidis	+	96.4
Enterobacter aglomerans (I)	-	90.6
Acinetobacter calcoaceticus	-	99.9
Enterobacter aglomerans (II)	-	69.0
Micrococcus sp. (II)	+	100.0
Micrococcus sp. (III)	+	99.9
Staphylococcus aureus (pigmented)	+	99.9
Staphylococcus aureus (nonpigmented)	+	99.9

Example III

To demonstrate applicability and durability to the skin, volunteers were used. TMS as a 0.42% water solution (A); TMS (14.4%) as the emulsifier of a volatile silicone in water diluted to 0.42% active in water (B); TMS (14.4%) as the emulsifier of polydimethylsilicone (PDMS), 50 centistokes, diluted to 0.42% active in water (C); and a water control (D); were swabbed onto the back of the left hand progressing up the anterior forearm as A, B, C and D of each test subject and allowed to air dry. Each test patch was approximately 3 cm by 6 cm. After drying, successive tape pulls of Scotch® Brand Magic™ Tape were made and colorimetric analyticals made by dipping the test tapes in a 0.25% Bromophenol blue solution for five minutes at ambient room temperature; rinsed in water; and dried. Readings were made based on bromophenol blue intensity on the tape. Affinity for and durability of TMS to the skin is demonstrated with greater penetration provided by the PDMS fluid and the greatest penetration by the volatile fluid preparation of the present invention.

The results of Example III are shown in Table X.

TABLE X

SKIN DURABILITY - TMS

Subject	Formulation/Tape Pull/Ratings			
	A. TMS Water BPB Rating 1, 2 Pulls	B. TMS Volatile BPB Rating Pulls	C. TMS PDMS BPB Rating Pulls	D. Water Control BPB Rating Pulls
	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
1. Male	H H L O O	H H H M L	H H M L O	O O O O O
2. Male	H H L L O	H H H M L	H M M O O	O O O O O
3. Female	H H L O O	H H H L L	H M M O O	O O O O O
4. Female	H H L O O	H H H L L	H M M O O	O O O O O

1. BPB - Bromophenol Blue
2. H = Very Dark Blue
   M = Medium Blue
   L = Light Blue
   O = No Color

Example IV

Antimicrobial activity against the organism associated with acne vulgaris, Propionibacterium acnes, was determined as follows. P. acnes was applied to Dacron fabrics that had been surface treated with the compositions A-D of Example III above.

The test compositions with TMS were swab applied to saturation on a 8 cm x 8 cm swatch of Dacron, dried at 100° C. for 15 minutes and tested using the American Association of Textile Chemists and Colorists - 100-1977 test, modified to include retrieval media suitable for growing the P. acnes. The results are indicated in Table XI.

TABLE XI

TMS COATED FABRICS AGAINST PROPIONIBACTERIUM ACNES				
Sample	A. TMS Water On Fabric	B. TMS Volatile On Fabric	C. TMS PDMS On Fabric	D. Water Control On Fabric
% Reduction P. acnes	99.99	99.96	99.98	0

In Examples II to IV and in Tables IX to XI, the term "volatile" has been used to indicate those materials previously indicated as the water immiscible liquids and PDMS is a fifty centistoke polydimethylsiloxane fluid, measured at 25° C.

The foregoing illustrates the activity of the compounds of the present invention. Such compounds have been found to be effective against a number of microorganisms, such as BACTERIA: Gram (-); Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca, Pseudomonas aeruginosa, Pseudomonas fluorescens, Proteus mirabilis, Proteus vulgaris, Salmonella typhi, Salmonella typhimurium, Salmonella cholera suis, Enterobacter cloacae, Enterobacter aerogenes, Morganella morganii, Aeromonas hydrophila, Citrobacter freundii, Citrobacter deversus, Serratia marcescens, Serratia liquifaciens, Xanthomonas campestris, Acinetobacter calcoaceticus; Gram (+): Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus mutans, Streptococcus pyogenes, Streptococcus fecalis, Micrococcus lutea, Bacillus sp. (vegetative cell); Fungi: Aspergillus niger, Aspergillus flavus, Aspergillus sydowi, Aspergillus versicolor, Aspergillus terreus, Penicillium chrysogenum, Penicillium variabile, Penicillium funiculosum, Penicillium pinophilum, Poria placenta, Aureobasidium pullulans, Gloeophyllum trabeum, Chaetomium globosum, Trichoderma viride, Trichophyton mentagrophytes; Fungi (yeasts): Candida albicans, Candida pseudotropicalis, Saccharomyces cerevisiae.

The treatment of skin disclosed herein can be carried out with the quaternary ammonium compounds of this invention per se. Often, however, it is desirable to extend the compounds of this invention by incorporating therein hydrocarbon or halohydrocarbon substituted siloxanes of the formula

$$\frac{R_aSiO_{4-a}}{2}$$

in which R is a hydrocarbon or halohydrocarbon radical and a varies from 0 to 3. The incorporation of such siloxanes in no way effects the property of the quaternary ammonium compound so that the claims of this invention are construed to cover both the use of quaternary ammonium siloxane per se and mixtures or copolymers of such siloxanes with said hydrocarbon substituted siloxanes or halohydrocarbon substituted siloxanes.

For example, surfaces can be treated with an aqueous solution of a mixture of 10 mols of monomethyl trimethysilane and 1 mol of

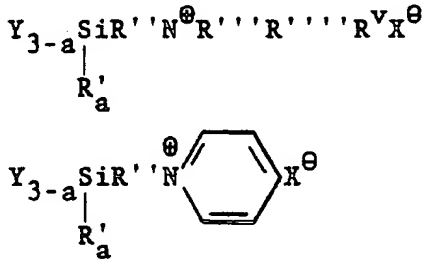
$Cl^-C_{18}H_{37}Me_2N^+(CH_2)_3Si(OMe)_3$.

It has also been found that combinations of 1 mol
$Cl^{-}C_{18}H_{37}Me_2N^{+}(CH_2)_3Si(OMe)_3$
and 0.5 mol of 3-chloropropyltrimethoxysilane give effective siloxane coatings. The use of hydrocarbon and halohydrocarbon siloxane extenders often give cheaper, more durable, more oleophilic or oleophobic surface treatments, than the pure quaternary siloxane.

It will be apparent from the foregoing that many other variations and modifications may be made in the compounds, compositions and methods described herein without departing substantially from the essential features and concepts of the present invention. Accordingly, it should be clearly understood that the forms of the invention described herein are exemplary only and are not intended as limitations on the scope of the present invention.

Claims

1. A method of treating acne vulgaris of the skin comprising applying topically to the epidermis a composition of an emulsion including an antibacterially effective amount of a silane and a water immiscible liquid, causing the silane to penetrate follicular orifices, driving the silane into sebaceous glands and destroying members of the staphylococcal group of bacteria therein, the silane being an organosilicon quaternary ammonium compound and an organosilane having the general formula selected from the group consisting of



and

wherein, in each formula,
Y is R or RO where each R is an alkyl radical of 1 to 4 carbon atoms or hydrogen;
a has a value of 0, 1 or 2;
R' is a methyl or ethyl radical;
R'' is an alkylene group of 1 to 4 carbon atoms;
R''', R'''' and R^{v} are each independently selected from a group consisting of alkyl radicals of 1 to 18 carbon atoms, $-CH_2C_6H_5$, $-CH_2CH_2OH$, $-CH_2OH$ and $-(CH_2)_xNHC(O)R^{vi}$, wherein x has a value of from 2 to 10 and R^{vi} is a perfluoroalkyl radical having from 1 to 12 carbon atoms; and
X is chloride, bromide, fluoride, iodide, acetate or tosylate.

2. The method of claim 1 wherein the water immiscible liquid is a polysiloxane selected from the group consisting of polysiloxanes having the general formula
$R'_3SiO(R''_2SiO)_w(R'''QSiO)_zSiR'_p3$ and $(R'R''SiO)_y$
wherein R' is an alkyl radical of 1 to 3 carbon atoms, phenyl, an alkoxy radical having the formula $R''''O-$, wherein R'''' is an alkyl radical of 1 to 4 carbon atoms or hydrogen; R'' is an alkyl radical of 1 or 2 carbon atoms or the phenyl group; R''' has the same meaning as R''; Q is a substituted or unsubstituted radical composed of carbon and hydrogen or carbon, hydrogen and oxygen or carbon, hydrogen and sulfur or carbon, hydrogen and nitrogen; w has a value of from 1 to 500; z has a value of 1 to 25 and y has a value of 3 to 5.

3. The method of claim 2 wherein the composition includes an abrasive selected from the group consisting of pumice, talc, mica, iron oxide, titanium oxide, titanium dioxide, zinc oxide, kaolin, magnesium oxide, zinc stearate, magnesium stearate, starch, chalk, magnesium carbonate and boric acid.

4. The method of claim 3 wherein the composition includes an astringent selected from the group consisting of alum, silver nitrate, aluminum sulphate, aluminum chlorohydrate, zinc chloride, zinc chlorohydrate, aluminum- zirconium chlorohydrate, aluminum chlorohydroxide, zirconium hydroxychloride, aluminum hydroxychloride-zirconyl hydroxy oxychloride and aluminum-zirconium tetrachlorohydrex-glycinate.